5.0 MECHANISTIC STUDIES

5.1 BODY OF EVIDENCE

The mechanistic body of evidence is extensive and is characterized by many isolated experiments using a variety of exposure conditions. The DHS reviewers and those in the NIHES Working Group did not find a pattern of evidence providing much clarification. In as much as the evidence is not easy to summarize concisely, the reader is referred to the NIEHS Working Group's review.

Nevertheless, the DHS reviewers felt that studies on chicken embryo developments under magnetic field exposure show a somewhat consistent pattern of results than may deserve further investigation. For a summary of these studies see Appendix Five.

5.2 PRO AND CON ARGUMENTS

TABLE 5.2.1 GENOTOXICITY AND REGULATION OF GENE EXPRESSION

AGAINST CAUSALITY	FOR CAUSALITY	COMMENT AND SUMMARY
(A1) There is no consistent pattern supporting genotoxicity.	(F1) If an effect is limited to a susceptible section of the general population, the small number of animals used in these studies may include few or NO susceptible subjects. This is a distinct possibility: Scarfi et al. (Scarfi et al., 1997) show increased micronuclei formation in lymphocytes from patients with Turner's syndrome (only one X chromosome) when the cells are exposed to pulsed but not to sinusoidal magnetic fields. No effect of these treatments is seen in lymphocytes from normal patients. The response of lymphocytes from Turner syndrome patients demonstrates the existence of at least one genetic subpopulation with greater sensitivity to specific types of EMF exposure. There may be other sensitive subpopulations. This problem is not encountered in epidemiological case-control studies or in sufficiently large cohort studies.	(C1) The evidence indicates that EMFs cannot be a cancer initiator, but is not relevant to the hypothesis that EMF is a risk factor at some stage of cancer OTHER than initiation.
(A2) Some positive results have been irreproducible even within the original laboratory.		(C2) The possibility that EMFs act only on a subset of the general population casts more doubts on the probative value of negative animal experiments.

AGAINST CAUSALITY	FOR CAUSALITY	COMMENT AND SUMMARY
(A3) There is overwhelming negative evidence against DNA damage and chromosomal effects.		(C3) True, but the risk of developing cancer does not depend only on the ability of damaging DNA.
(A4) There are consistently negative results of mutagenesis below 0.1–1 mT.		
(A5) Any reported effect resulted from exposure to fields is orders of magnitudes above environmental levels.		

TABLE 5.2.2 SIGNAL TRANSDUCTION

AGAINST CAUSALITY	FOR CAUSALITY	COMMENT AND SUMMARY
(A1) Most of the positive results come form single laboratories and have not been independently replicated.	(F1) Results indicate that magnetic fields ≥ 0.1 mT and electric fields ≥ 1mV/m have effects on a number of signal transduction-related pathways in mammalian cells.	(C1) It is not clear how these results influence the interpretation of epidemiology.
(A2) The physiological significance of blocking of antiproliferative effects of melatonin or Tamoxifen, published by three laboratories (Liburdy et al., 1993), (Blackman et al., 2001), (Ishido et al., 2001) is unknown. The effect is very weak.	(F2) The blocking of antiproliferative effect of melatonin at 1.2 μT has been published by three labs. This suggests the possibility of bioeffects at intensities where biophysical theory suggests that no bioeffect would be expected.	(C2) Any replicated biological effect at exposure levels comparable to those in the environment increases the credibility of the hypothesis. Moreover, effects on cell proliferation are relevant to cancer and reproductive health. These findings need to be replicated and published from other labs.
(A3) There is no clear pattern of effects.		(C3) Failure to find cell physiological responses to high intensity or near residential intensity fields is unsupportive of the hazard hypothesis. But there is the usual problem of testing a complex mixture on special cell preparations so that the sensitivity of the test is not great. Many agents will not cause effects observable in the laboratory at ambient levels of concentration. Those agents often have linear dose response so that high doses produce obvious effects. Epidemiological evidence suggests that this may not be true for EMFs.
(A4) Positive results have been achieved only with prolonged exposure to strong (>50 uT) fields.		

5.3 CONCLUSIONS

Overall, the picture is mixed and does not affect the DHS reviewers' confidence level much.

The blocking of antiproliferative effect of melatonin at 1.2 uT, that has been published by three independent labs, increases the level of certainty, but not by much. The lack of replicated in vitro reactions to pure 60 Hz fields at near ambient levels and the lack of an understanding of a chain of mechanisms leading from exposure to pathology is an evidentiary deficiency, but this stream of evidence often is prone to false negatives. If positive results are present, they increase confidence a lot, but their absence decreases it only a little.